

WE CLAIM:

5 1. A modified antiangiogenic peptide comprising a reactive group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form stable covalent bonds wherein said reactive group is selected from the group consisting of succinimidyl and maleimido groups.

10 2. The as modified peptide of claim 1 wherein said peptide is a kringle 5 peptide.

15 3. A kringle 5 peptide according to claim 2 wherein said derivative is reactive with blood proteins.

20 4. A kringle 5 peptide according to claim 3, wherein the derivative is reactive with a thiol group on a blood protein.

25 5. A kringle 5 peptide according to claim 2 wherein the peptide is selected from the group consisting of SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.

30 6. A kringle 5 peptide according to claim 2 wherein the peptide is selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16.

35 7. A composition comprising a derivative of kringle 5 peptide or analog thereof, said derivative comprising a reactive group which reacts with amino groups, hydroxyl groups or thiol groups on blood components to form stable covalent bonds wherein said reactive group is selected from the group consisting of succinimidyl and maleimido

groups for use in a method of treating angiogenesis in a human.

8. The composition of claim 7 wherein said derivative is reactive with blood proteins.

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9. The composition of claim 7 wherein said derivative is reactive with a thiol group on a blood protein.

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10. A derivative of a kringle 5 peptide, said derivative comprising a maleimido group which reacts with a thiol group on human serum albumin to form a covalent bond.

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11. The derivative of claim 10 wherein said peptide is selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 and SEQ ID NO:9

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12. The derivative of claim 10 wherein said peptide is selected from SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16.

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13. A composition comprising a derivative of an anti-angiogenic peptide, said derivative comprising a maleimido group which reacts with a thiol group on human serum albumin to form a covalent bond for use in a method of treating angiogenesis in a human.

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14. The composition of claim 13 wherein the peptide is a kringle 5 peptide.

15. The composition according to claim 14, wherein the peptide is selected from SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8 and SEQ ID NO:9.

16. A composition according to claim 14 wherein the peptide is selected from SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15 and SEQ ID NO:16.

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17. Use of a composition for the manufacturer of a medicament extending the *in vivo* half-life of a kringle 5 peptide in a patient to provide an anti-angiogenic effect, the composition comprising a derivative of a kringle 5 peptide or analog thereof, said derivative comprising a reactive group which reacts with amino groups, hydroxogroup, or thiol groups on blood components to form stable covalent bonds, wherein the reactive group is selected from the group consisting of succinimidyl and maleimido groups.

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18. Use of a composition according to claim 14, wherein the derivative is reacted with blood proteins.

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19. A modified kringle 5 peptide selected from the group consisting of NAc-Pro-Arg-Lys-Leu-Tyr-Asp-Lys-NH₂; NAc-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-NH₂; Nac-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-NH₂; NAc-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-Ala-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-NH₂; NAc-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-Lys-NH₂; NAc-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-(Nε-MPA)-NH₂; (MPA-AEEA)-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂ and (MPA)-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂.

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20. A modified kringle 5 peptide selected from the group consisting of: NAc-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-(Nε-MPA)-NH₂; (MPA-AEEA)-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂; (MPA)-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂; NAc-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-Ala-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-(Nε-MPA)-NH₂;

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(MPA-AEEA)-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-Ala-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂; and
(MPA)-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-Ala-Tyr-Thr-Thr-Asn-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂.

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21. 20. A modified kringles peptide selected from the group consisting of NAc-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-Lys-(N_ε-MPA)-NH₂; (MPA-AEEA)-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-NH₂;

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(MPA)-Arg-Asn-Pro-Asp-Gly-Asp-Val-Gly-Gly-Pro-Trp-NH₂;

NAc-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-(N_ε-MPA)-NH₂;

(MPA-AEEA)-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂;

(MPA)-Arg-Lys-Leu-Tyr-Asp-Tyr-NH₂;

NAc-Pro-Arg-Lys-Leu-Tyr-Asp-Lys-(N_ε-MPA)-NH₂;

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(MPA-AEEA)-Pro-Arg-Lys-Leu-Tyr-Asp-NH₂;

(MPA)-Pro-Arg-Lys-Leu-Tyr-Asp-NH₂;

NAc-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-(N_ε-AEEA-MPA)-NH₂; and

NAc-Pro-Arg-Lys-Leu-Tyr-Asp-Tyr-Lys-(N_ε-AEEA_n-MPA)-NH₂.